Stickler. (J.W.)

FOOT-AND-MOUTH DISEASE

AS IT AFFECTS MAN AND ANIMALS, AND ITS RELATION TO HUMAN SCARLATINA AS A PROPHYLACTIC

ALSO, REMARKS UPON THE TRANSMISSION OF HUMAN SCARLATINA TO THE LOWER ANIMALS, AND THE USE OF VIRUS THUS CULTIVATED AS A PREVENTIVE AGENT

BY

J. W. STICKLER, M.S., M.D.

ORANGE, N. J

SURGEON GENERAL'S OFFICE
331
LIBRARY

Reprinted from THE MEDICAL RECORD, *December* 10, 1887

NEW YORK
TROW'S PRINTING AND BOOKBINDING CO.
201-213 EAST TWELFTH STREET
1887

FOOT-AND-MOUTH DISEASE

AS IT AFFECTS MAN AND ANIMALS, AND ITS RELATION TO HUMAN SCARLATINA AS A PROPHYLACTIC

ALSO, REMARKS UPON THE TRANSMISSION OF HUMAN SCARLATINA TO THE LOWER ANIMALS, AND THE USE OF VIRUS THUS CULTIVATED AS A PREVENTIVE AGENT

BY

J. W. STICKLER, M.S., M.D.

ORANGE, N. J

SURGEON GEN'L'S OFFICE LIBRARY 331

Reprinted from THE MEDICAL RECORD, *December* 10, 1887

Presented by the author

NEW YORK
TROW'S PRINTING AND BOOKBINDING CO.
201-213 EAST TWELFTH STREET
1887

FOOT-AND-MOUTH DISEASE AS IT AFFECTS MAN AND ANIMALS, AND ITS RELATION TO HUMAN SCARLATINA AS A PROPHYLACTIC.

Also, Remarks upon the Transmission of Human Scarlatina to the Lower Animals, and the Use of Virus thus Cultivated as a Preventive Agent.

The disease as it affects man.—It was long ago discovered that the human subject was susceptible to the contagium of foot-and-mouth disease. The disease is contracted in one of two ways, viz., by drinking milk obtained from cows affected with the disease, or by the accidental introduction of the virus into open wounds or sores upon the hands, or other parts of the body. In either case the systemic disturbance is, as a rule, very slight, while the local lesion, in the great majority of instances, consists of an inflammatory sore throat, with or without the development of small vesicles upon the inner surface of the cheeks, lips, and tongue. The cervical lymphatic glands are generally enlarged and tender. The tongue sometimes becomes swollen to a considerable degree. In some instances there has been an eruption of vesicles upon the feet and hands, in others a scarlet eruption has made its appearance upon different parts of the body. Hertwig,[1] during an epidemic of foot-and-mouth disease, drank daily for four days one quart of milk taken from diseased cows. In less than forty-eight hours he "began to experience slight fever, twitchings in the limbs, headache, a sensation of dryness and heat in the mouth, and an itching in the hands and fingers. These symptoms continued about five days.

[1] Ziemssen's Cyclopædia of the Practice of Medicine, vol. iii., p. 521.

Then the entire mucous membrane of the mouth began to swell considerably, especially that of the tongue, upon which organ, particularly the edges of it, and also upon the inner surface of the cheeks and lips, there appeared small vesicles, never larger than a lentil, of a yellowish-white color, and filled with turbid whitish contents which were readily discharged when the vesicles were pricked, but were soon reproduced. Upon the following days the vesicles became still larger, and burst; the epithelium was then detached, leaving behind dark-red erosions which gradually healed. There was, conjoined with the above symptoms, a smarting pain in the mouth upon the attempt to masticate, speak, or swallow, and also an intense thirst. The vesicles upon the lips dried up, leaving in their places thin brown scurfs, which upon the tenth day after the appearance of the former fell off. Simultaneously with the development of the eruption in the mouth, numerous vesicles were formed upon the hands and fingers, which at first were of the size of a millet-seed, firm, and of a yellowish-white color, but in their further progress approximated in look to those in the mouth, healing, however, more slowly. At the termination of this process he was restored to the best of health." Two other physicians performed the same experiment upon themselves, with the same result as obtained in the case of Hertwig, except that they had no eruption of vesicles upon their hands. The symptoms thus produced by drinking fresh milk containing the contagium of the disease under consideration, vary somewhat from those produced by inoculation of the human subject with the contents of the vesicles, at least in some instances. That this is true will be shown in the record of the following cases:

About the end of August,[1] Mrs. X——, wife of an extensive farmer, came under my care on account of an eruption of *bright red spots*, one-eighth of an inch in diameter

[1] Edinburgh Medical Journal, 1863, Hislop.

(covered with a thin white desquamation), which were so densely sprinkled over her body as to leave only minute interspaces of sound skin. As Mrs. X—— had within the last three years suffered from hepatitis with jaundice, I thought the eruption might be thus originated. Alterative purgatives made no impression upon the disease.

On a subsequent visit I found her husband complaining of a sore throat and mouth. Upon examination found the mucous membrane of his mouth, lips, tongue, and throat studded with small ulcers, giving off a white slough, which left behind a clean but highly sensitive cup-shaped cavity. His forehead was covered with an eruption similar to that upon the lower extremities of his wife. The eruption was never vesicular as it is in cattle. The spots made their appearance as slightly elevated, reddish prominences (papulæ), which gradually became bright red, then threw off a silvery-white scale, and gradually disappeared. Mrs. X—— had slight inflammation of the fauces. Some of the children about the house were also affected with sore throat, but the symptoms in these cases were very mild and easily overcome. At the time this disease affected the above patients the whole of Mr. X——'s cows had murrain. Mr. X—— says that, when examining one of the cows which was suffering from the disease, and while in the act of pressing back the lip, he observed two or three pimples on the upper lip to burst and eject the matter to a considerable distance, and that he received a portion on his cheek and hand. Both parties, as well as those affected in a lesser degree, had gone freely about the byres, handling the diseased cows, of which there were at times upward of a dozen ill at once, and the peculiar virulence of the symptoms in Mr. X——'s case seemed to depend upon the circumstance that the matter caught upon his hand and cheek was derived from one of the worst of the diseased animals. The epidemic of "sore throat" which occurred at Dover, England, in 1884, furnishes still greater opportunity for the study of "foot-and-mouth disease" as

it affects man.[1] "During the early days of February, 1884, a remarkable outbreak of sore throat occurred in Dover, England, which, on account of the suddenness of the outbreak, the severity of the symptoms, and its chief prevalence among those occupying the best houses in the town, attracted no small amount of public attention, and naturally provoked a large amount of interest in the investigation as to the cause thereof. Controversy waxed warm, especially when it became known that the course of the epidemic corresponded most intimately with the track of a particular milkman, and that the milk supplied by this man was believed to be the vehicle of the specific poison occasioning the epidemic. . . . For the purpose of ascertaining what particular taint was present in the milk which was calculated to occasion this particular epidemic, a searching inquiry was made, and the following facts collected: The implicated dairyman obtained his supply of milk from twelve cows kept on his own premises at Dover, and also from three farm establishments in the country. All these places were visited and diligent search made for any evidence of the disease among either the cows or people living or engaged on the premises.

"At one of the establishments in the country it was found that aphthous fever had broken out among the stock on January 14th, and that milk from some of the affected cows was delivered to the Dover dairyman, and, after being mixed with other milk, distributed to his customers. Moreover, it was from this infected farm alone that the Dover dairyman obtained the supply of cream furnished to his customers. At the beginning of the inquiry it was stoutly denied that any of the milch-cows had suffered from disease, and a certificate from a veterinary surgeon and inspector to this effect was obtained and published. The matter was then referred to the police, and the truth gradually oozed out, until the facts as

[1] Quoted from the official report of the epidemic.

already stated were established beyond dispute; then the farmer not only admitted the fact of the disease among the milch-cows, but confessed to the sale of their cream and milk in Dover, not only to the dairyman whose milk was especially implicated, but also to another milkman, on two separate occasions, among whose customers a second simultaneous outbreak occurred; thus a second experiment was performed with this tainted milk among another set of individuals, with like results to the first, contributing additional evidence of the presence of poison in the milk supplied from the infected farm. Thus it was clearly established that the sufferers in this epidemic partook of milk which had been secreted by cows suffering from foot-and-mouth disease. During the week ending February 9th, two hundred and five persons were attacked with this disease. The majority of persons who suffered during the Dover epidemic presented two prominent symptoms in common, viz., *inflammatory sore throat and enlargement of the cervical lymphatic* glands; but the lesions produced varied considerably in different cases. The vesicular eruptions were followed either by a raw, red, œdematous appearance of the mucous membrane, or white patches, and the ulcers which supervened assumed in many instances a chronic character, with thick, puckered edges, and were a long time in healing. When the inflammation went on to suppuration recovery was much slower than after common quinsy, and the enlarged cervical glands remained tender, red, and swollen long after the throat symptoms had subsided, *resembling in this respect the sequelæ of* scarlet fever. Erysipelas and purulent formations were also concomitants of the epidemic. In some instances the feet of those who suffered were swollen and painful, simulating rheumatism; and in one instance eczema occurred between the toes of the feet, the affection being accompanied with very fetid exhalation. A fatal termination resulted in the cases of two children who had very bad throats and mouths, with the extension of the disease to

the respiratory tract, their deaths being, in the opinion of the medical attendant, due to the poisonous effects of the milk. Two persons, who labored under chronic kidney disease, were respectively attacked with sore throat and died on the same day; other people in the same houses suffering also from the epidemic sore throat."

Having thus traced the course of foot-and-mouth disease as it occurred in the cases quoted, and thinking it manifested a certain resemblance to human scarlatina, I asked Dr. M. K. Robinson, medical officer of health of East Kent, England, if he would call upon the various persons who had been affected with the "epidemic sore throat," and ask them whether they had had scarlet fever either before or after having the "sore throat" in 1884, my object being to determine whether the human system, having been attacked by one of these diseases, would, as a result, become fortified against the contagium of the other.

TABLE.

Incidence of Scarlet Fever among Persons who Suffered from "Epidemic Sore Throat" due to Use of Milk derived from Cows Suffering from Aphthous Fever, which Epidemic occurred in Dover in 1884.

No. of case.	Scarlet fever previously.	Scarlet fever since.	Remarks.
1	.....	.....	Four other members of same family, who had previously had scarlet fever, escaped epidemic of sore throat.
2	.....	.....	
3	.....	.....	
4	.....	.....	Five other members of this family, who had previously had scarlet fever, escaped throat epidemic.
5	1	.....	
6	.....	.....	
7	.....	.....	Two members of same family, who had previously had scarlet fever, escaped throat epidemic.
8	1	.....	
9	.....	.....	

TABLE.—*Continued.*

No. of case.	Scarlet fever previously.	Scarlet fever since.	Remarks.
10	1 ?	.....	Believed to have had scarlet fever with other members of family when young.
11	?	?	Gone away, no address to be found.
12	.....	.....	
13	.....	.....	
14	.....	.....	
15	?	?	Gone away, no address yet found.
16	?	?	
17	?	?	
18	.....	.....	
19	1 ?	.....	Not quite certain, but thinks to have had scarlet fever when young.
20	?	?	Gone away, address not yet found.
21	.....	.....	
22	.....	.....	
23	.....	.....	
24	.....	.....	
25	1	.....	Believed to have had scarlet fever when young.
26	.....	.....	
27	.....	.....	
28	?	?	Gone away, address not yet ascertained.
29	.....	.....	
30	1	.....	
31	.....	.....	
32	.....	.....	Same family.
33	.....	.....	
34	1	.....	Same family, 34 had scarlet fever when young; 35 uncertain.
35	?	.....	
36	.....	.....	Same family.
37	.....	.....	
38	?	?	Same family. Gone away, address not yet ascertained.
39	?	?	
40	?	?	Same family. Gone away, address not yet found.
41	?	?	
42	.....	.....	Same family. Other members of same family, two of whom had had scarlet fever, escaped epidemic sore throat.
43	.....	.....	
44	?	?	Same family. Gone away.
45	?	?	
46	.....	.....	Same family.
47	.....	.....	
48	.....	.....	Same family.
49	.....	.....	
50	1	.....	Same family.
51	1	.....	

TABLE.—*Continued.*

No. of case.	Scarlet fever previously.	Scarlet fever since.	Remarks.
52	?	?	Same family. Gone away, address not yet found.
53	?	?	
54	.....	.....	Same family.
55	.....	.....	
56	.....	.....	Same family.
57	.....	.....	
58	.....	.....	Same family.
59	.....	.....	
60	.....	.....	Same family.
61	.....	.....	
62	.....	.....	Same family.
63	.....	.....	
64	.....	.....	Same family.
65	.....	.....	
66	1	.....	66 scarlet fever or measles, not quite certain.
67	.....	.....	
68	.....	.....	Same family.
69	.....	.....	
70	?	?	Same family. Gone away, address not yet found.
71	?	?	
72	.....	.....	Same family.
73	.....	.....	
74	.....	.....	Same family; consists of four children; one child, who had previously had scarlet fever, escaped epidemic sore throat.
75	.....	.....	
76	.....	.....	
77	1	.....	Mild case of throat epidemic.
78	.....	.....	
79	.....	.....	
80	.....	.....	Same household. Father, mother, and servants, who had previously had scarlet fever, escaped throat epidemic.
81	.....	.....	
82	.....	.....	
83	.....	.....	Same household.
84	.....	.....	
85	?	?	Servant, cannot be found.
86	.....	.....	
87	.....	.....	
88	.....	.....	
89	.....	.....	
90	.....	.....	Same family.
91	.....	.....	
92	1 ?	.....	Mother thinks they had scarlet fever.
93	1 ?	.....	
94	1 ?	.....	
95	.....	.....	Same family.
96	.....	.....	
97	?	?	Servant, cannot be found.

TABLE.—*Continued.*

No. of case.	Scarlet fever previously.	Scarlet fever since.	Remarks.
98	?	?	
99	?	?	Servants, cannot be found.
100	?	?	
101	.....	.....	
102	.....	.....	Same family.
103	.....	.....	
104	.....	.....	
105	.....	.....	Same family.
106	.....	.....	
107	.....	.....	
108	.....	.....	Same family.
109	.....	?	Servant, gone away.
110	.....	.....	Same household. Other members of this
111	.....	.....	family, three of whom had had scarlet
112	.....	.....	fever, escaped throat epidemic.
113	.....	.....	
114	.....	.....	Same household.
115	1	.....	
116	.....	.....	
117	.....	.....	Same household.
118	.....	.....	
119	.....	.....	
120	.....	.....	Same household.
121	.....	.....	
122	.....	.....	
123	.....	.....	
124	.....	.....	Same household.
125	.....	.....	
126	.....	.....	
127	.....	.....	
128	.....	.....	
129	.....	.....	
130	.....	.....	
131	1	.....	Mild case of throat epidemic.
132	.....	.....	Same household.
133	.....	.....	
134	.....	.....	
135	1	.....	
136	1	.....	Same household.
137	.....	.....	
138	.....	.....	
139	.....	.....	
140	.....	.....	Same household.
141	.....	.....	
142	.....	.....	
143	.....	.....	Same household.
144	.....	.....	

TABLE.—*Continued.*

No. of case.	Scarlet fever previously.	Scarlet fever since.	Remarks.
145	.....	.....	Same household.
146	.....	.....	
147	.....	.....	Same household. Other members, four of whom had had scarlet fever, escaped throat epidemic.
148	.....	.....	
149	.....	.....	
150	.....	.....	
151	?	.....	Servant, thinks had scarlet fever.
152	1	.....	
153	1	.....	
154	.....	.....	Same household; mild cases of throat epidemic.
155	.....	.....	
156	.....	.....	
157	.....	.....	
158	.....	.....	
159	.....	.....	Same household.
160	.....	.....	
161	.....	.....	
162	.....	.....	
163	.....	.....	
164	.....	.....	Same household.
165	.....	.....	
166	1	.....	
167	1	.....	
168	.....	.....	
169	.....	.....	Same household.
170	.....	.....	
171	.....	.....	
172	.....	.....	
173	.....	.....	
174	.....	.....	
175	.....	.....	Same household.
176	.....	.....	
177	.....	.....	
178	.....	.....	
179	.....	.....	
180	.....	.....	
181	?	.....	
182	?	.....	
183	?	.....	
184	.....	.....	
185	.....	.....	
186	.....	.....	
187	.....	.....	Same family. Removed. No reply to inquiry.
188	.....	.....	
189	.....	.....	
190	.....	.....	

TABLE.—*Continued.*

No. of case.	Scarlet fever previously	Scarlet fever since.	Remarks.
191	.....	.....	
192	.....	.....	
193	.....	.....	
194	.....	.....	
195	.....	.....	
196	.....	.....	
197	?	.....	Doubtful; do not think they had scarlet fever.
198	?	.....	
199	.....	.....	
200	.....	.....	
201	.....	.....	
202	.....	.. ...	
203	.....	.....	
204	.....	.....	
205	.....	.....	

These statistics were gathered two years after the outbreak of the "sore-throat epidemic" in Dover. During this interval of two years 22 of the patients changed the place of their residence and could not be found, with but few exceptions, and from these few it was impossible to secure replies. The tabulated facts concerning the remaining 183 persons show:

1st. That *none* of the persons affected with the "throat epidemic" have since had scarlet fever, *i.e.*, had not had it at the time they were questioned.

2d. *That members of eight families who had previously had scarlet fever escaped the "throat epidemic,"* while the remaining portion of the households developed the disease.

3d. That 16 persons affected with the "throat epidemic" had had scarlet fever.

4th. That 4 of the 16 persons who had had scarlet fever had a *mild form* of the "throat epidemic."

5th. That of the affected individuals 2 had had scarlet fever *when young.*

6th. That 10 of the cases were doubtful whether they had previously had scarlet fever.

May it not, therefore, be possible :

1st. That the affected persons have not since had scarlet fever because of the protective influence produced by the "throat epidemic."

2d. *That the members of certain households who had had scarlet fever had thereby secured immunity from the "throat epidemic," as indicated by the fact that they escaped.*

3d. That in four of the instances in which scarlatina had antedated the "throat epidemic" there was a partial protection afforded, as indicated by the fact that four of these cases were mild.

4th. That in those instances in which scarlatina had occurred in early youth the protection had become exhausted.

5th. That these two diseases may be for a time mutually protective.

It is certainly a remarkable fact that, in twenty-four or more instances, the throat epidemic failed to attack those who had already had scarlatina; also, that the few attacked with the throat epidemic who had had scarlatina, had, in one-fourth of the instances, a mild type of the epidemic disease, indicating, possibly, that the system had been so affected by the scarlatinal contagium as to become less susceptible to the virus of foot-and-mouth disease. That a certain number who had previously had scarlet fever were attacked by the "throat epidemic," is not strange, for it sometimes happens that an individual will have two attacks of scarlet fever, with, in some instances, only a short interval of time between the attacks. On the other hand, it may be true that the twenty-four or more individuals who had had scarlatina, and escaped subsequently the sore-throat epidemic, were not susceptible to the influence of the contagium which the infected milk contained. As is very well known, there are some persons who, though many times exposed

to the poison of small-pox, measles, or scarlatina, remain unaffected by such exposure. In considering the facts before us I think this truth should have its share of thoughtful attention.

Believing, however, that in the evidence furnished by the "Dover epidemic" there was an indication of what might possibly be accomplished by the use of the virus of foot-and-mouth disease as a preventive of human scarlatina, I made further experimental investigation, as follows:

With some virus (contents of vesicles) taken from cows having a mild form of foot-and-mouth disease, I inoculated three children, and subsequently exposed them to scarlet fever contagium. The histories given briefly will show the results:

Case I.—M. M——, about eight years of age; had never had scarlet fever. On January 12, 1884, I injected under the skin of his arm a small quantity of the virus. A short time thereafter the cervical lymphatic glands became enlarged and tender to the touch. There was no marked systemic disturbance, neither was there any sore mouth or throat. All signs of glandular enlargement and tenderness had disappeared in six or seven days. He was then taken to a house in which there was a boy sick with scarlet fever. The disease was in the desquamating stage and the throat still sore. His parents being poor, the pillow upon which the patient lay had not been exchanged for a clean one since the beginning of the sickness. This pillow was placed over the face of the boy who had been inoculated, and held there some time. He was then made to inhale the breath of the patient, and afterward to remain some time in the sick-room. The boy did not develop scarlatina after having been thus exposed, neither has he contracted the disease since, although there has been opportunity for infection.

Case II.—B. P——, aged four years; had never had scarlatina. On March 6th I inoculated her in the arm (hypodermically) with a small quantity of the foot-and-

mouth virus. On March 13th her temperature rose to 103° F. Her mouth was sore, without showing any vesicles, and she complained of a pricking sensation in her throat. She had slight headache, the appetite was impaired, and she was quite peevish. There was no eruption at any point on the body. By March 20th she was well. She was then taken to a house where I had a patient in the desquamating stage of scarlet fever. The patient was very sick at the time because of complications; indeed was so ill that I was somewhat doubtful about the issue. The same plan of exposure was adopted as in the first case, although I could not succeed in getting the inoculated child quite near enough to the patient to inhale her breath; but the "pillow exposure" and the length of time she remained in the sick-room afforded a good opportunity for infection. She did not subsequently develop scarlet fever.

CASE III.—J. M——, aged about ten years; had never had scarlatina. I inoculated him just as I did the first two. He did not afterward develop any systemic disturbance or local lesion. After a lapse of three years, with opportunity for infection, he tells me he has not had scarlatina.

The results thus obtained, especially when taken in connection with the data furnished by the statistical table, *seem* to furnish some reason for believing that, for a time at least, the virus of foot-and-mouth disease is protective against the contagium of human scarlatina. But I am well aware that at this stage of the investigation *conclusions* cannot, ought not to be advanced, and until further information can be obtained by careful experimental investigation, nothing absolute or positive should be said concerning the practical issue above alluded to. While foot-and-mouth disease, as it affects man, is in many respects the exact counterpart of the disease as it occurs in cattle, yet there are certain points of difference, and in order to make them apparent a brief description of the latter affection will be given. The disease (as it

affects cattle) may be defined as a very contagious and infectious affection, characterized by an eruption of vesicles or blisters in the mouth, on the internal surface of the lips, sometimes in the nostrils, on the teats and udder, between the pedal digits and around the coronets, and sometimes in the lactiferous ducts. It passes through four different stages, viz.: fever, eruption, ulceration, desiccation and desquamation. The symptoms of these four stages or periods are as follows:

First Period. Before any perceptible alteration has taken place in the ordinary habits or condition of the animal, the thermometer indicates an increase of temperature, which generally ascends to 102°, and as high as 104° or even 107° F., in from one to two days, and does not descend to any extent until the end of the eruptive period. The next indication is dulness, inappetence, and slight shiverings. The muffle becomes warm and dry, the eye is tearful, and the mouth hot and inflamed-looking in places, and frequently sore when handled, the membrane being covered with viscid mucus, which flows in stringy masses from the lips. There is grinding of the teeth, and a smacking or clicking noise; the breath has a fetid odor; rumination ceases, and the prehension, and often the deglutition, of food is painful, the animal preferring to dabble its mouth in cold water. Not infrequently, when the feet are beginning to inflame, the animal stands uncomfortably, drawing the limbs together, or jerking them up suddenly under the body, arching the back, and pawing; the movements are reluctantly performed, and the coronets hot and sore. There is also slight constipation, and, if with a milch-cow, the secretion of milk is gradually diminished, and that fluid assumes a yellow tint; in the majority of cases it is nearly or altogether suspended. *The udder becomes red and tense* when it is involved, and the teats swollen and painful to the touch. This stage usually lasts from twenty-four to forty-eight hours, according to the intensity of the fever.

Second Period. After the time above mentioned the

eruption begins to appear in those parts which are to be its seat, and the fever commences to abate in many cases. When the mouth is chiefly affected there are seen on its lining membrane, and particularly on the upper lip, gums, and sides of the tongue and palate, white or yellowish-white blisters, the size of a grain of millet to that of the size of a pea or nut, their form being very irregular. Sometimes they are discrete, or scattered over the surface; in other cases they are confluent, collectively forming patches which are at first gray or yellow, and afterward white; slightly convex; each vesicle is usually circular; the smallest are seen on the muffle. In the mouth they are largest, and most frequently confluent; but there they only exist for a brief period, the friction caused by the movements of the tongue tearing them; the epithelium is detached in flakes of variable dimensions, leaving unhealthy ulcers or denuded spots, or "erosions" of a bright red tint, which contrasts markedly with the gray hue of the surrounding surface. These shreds are often seen adhering to the border of these sores; and if on the tongue, that organ is kept continually moving to get rid of them, and the animal emits a smacking sound with its lips. At this stage of the disease the papillæ of the tongue are congested and prominent. Where there is no friction the vesicles do not rupture within one or two days. On the udder the vesicles are somewhat different. *The teats are most frequently their seat,* and it is not unusual to find the phlyctenæ grouped in a circle around their orifice; when isolated on the surface of the organ they are surrounded by a pale-red circle, and when confluent they are very irregular and variable in number. In the case of a cow the alteration of the milk is very striking. It coagulates on being boiled, or when its temperature is only slightly raised. It also becomes yellow in color and acid in reaction.

When the limbs are affected the heat and redness of the coronet are most noticeable toward the heel and inter-

digital space of one or more feet. The coronet swells; the animal is lame, and prefers to maintain a recumbent position. In one or two days the vesicles are developed at the points indicated, most frequently earliest in the interdigital space; at first they are small, but they increase in size until they are as large as a bean or small nut, and extend round the claws, often becoming confluent, the contents appearing as a yellow limpid fluid. The skin of the part assumes a bleached aspect, and is soon covered with a kind of cheesy matter, resulting from the inspissation of this fluid, which emits an ammoniacal odor. In some cases the skin around the base of the horns becomes inflamed at the same time as that of the mouth or feet, and the horns are loosened. Occasionally, also, a vesicular eruption manifests itself at the orifice of the vagina, at the perineum and anus, or in the nostrils; and it sometimes happens that the eyes are affected, the conjunctival membrane becoming inflamed and suppurating, and phlyctenæ forming on the cornea. There may also be nasal catarrh and symptoms of gastric derangement.

Third Period. This is the aphthous stage of the disease, and begins when the vesicles have ruptured, and, the epidermis being removed, erosions appear. This does not occur everywhere at the same time, but varies according to the region. In the mouth it soon occurs, owing to the movement of the tongue, and also in the feet by that of the claws. On the udder it is later, seldom occurring before thirty-six or forty-eight hours; or if the disease is benignant the vesicles on this organ may not rupture at all, their contents becoming absorbed, and the pellicle of epidermis covering them scaling off when cicatrization has taken place beneath. When the vesicles do break, there remains a little, bright-red sore, which is smooth or granulating, and is soon covered with a fluid pus mixed with epithelial cells, which in drying forms a thin reddish crust that protects the erosion until it heals. In the mouth and on the lips the vesicles are

broken almost as soon as formed, leaving circular or irregular bright-red sores which bleed readily, their rupture being indicated by dribbling of saliva streaked with blood.

It sometimes happens that when the tongue is seized to explore the mouth, large patches of epidermis come away in the hand, as if the tongue had been boiled. In some rare cases an exudation of yellow color and cheesy consistency is observed toward the root of the tongue, due to epithelial proliferation.

The fever has greatly subsided, but the thirst is intense, and the animal eagerly drinks water or gruel, though, owing to the soreness of the mouth, it can eat but little, especially if the food be dry and hard; consequently the loss of condition is rapid.

Fourth Period. This is marked by the desiccation or drying up of the aphthæ, and the formation of new epidermis. The crust falls off, and new epidermis or epithelium appears as a thin, lead-colored pellicle. There is also at this time a general desquamation of the cuticle, and this is invariably the case. There is also a good deal of itching of the surface (Walley). With the completion of these processes all traces of the disease disappear. There is no lameness, the appetite has returned, and the former condition is being restored; while the secretion of milk, which may have been greatly diminished—perhaps to less than one-third—becomes augmented, and regains its normal properties.

Bollinger states that "in animals which have once acquired the disease the susceptibility ceases for a considerable period, or at least becomes very slight. Repeated attacks of the malady in the same animal are, upon the whole, rare." That the susceptibility ceases for a time has been demonstrated by Dr. E. Klein, of London, England. He inoculated five sheep with active cultivations of the micrococcus, but without producing any definite local or general lesion. "Subsequent feeding of these same sheep with the active micrococcus had no result."

From this he argues that a previous subcutaneous inoculation with the micrococcus provides the animals with immunity against the disease. Dr. Klein also claims to have discovered the germ peculiar to this disease. His method of investigation was as follows: He inoculated alkaline peptones, broth, and solid agar-agar, peptone broth mixture, solid nutritive gelatine mixture, and milk, with lymph which was obtained from the vesicles of diseased sheep. He discovered, after a few days, a thin film, limited in extent, upon the surface of the solid media at and near the point of puncture. The film gradually spread, presenting a very characteristic appearance, namely, *a collection of closely packed minute granules* or droplets. These enlarge slowly and gradually, and become whitish and translucent in character. If the point of a needle or platinum wire be moistened with the lymph and pushed into the solid medium, the line of puncture becomes marked as a linear aggregation of minute granules or droplets after several days or weeks. There is also, in addition to this, on the surface of the culture media the film of granules already alluded to, which starts from the point of inoculation. This micrococcus grows very slowly, the first indication of its growth in solid nutritive gelatine mixture, at a temperature of 18° to 22° C., becoming visible under a lens at the end of from five to eight days, or still later. The growth thus developed appears in the form of a small cluster of transparent granules. In agar-agar mixture, kept at 35° to 38° C., the growth is sooner visible, although, after six or seven months, "in all media and under all conditions the growth remains of limited extent." When milk is inoculated with the micrococcus, and kept at a temperature varying between 35° and 38° C., the growth is found to progress very slowly. The condition and natural appearance of the milk are not changed. No curdling occurs, but the reaction becomes acid. The micrococcus forms in artificial media dumb-bells (diplococcus) and beautiful chains (streptococcus). These vary in length

according to the number of micrococci composing them, "the short chains being a linear series of four, six, or eight micrococci, the longer ones of more than eight up to thirty and more micrococci." The longer chains are always curved, and even convoluted.

The above-mentioned characteristic appearance of the growth is owing to the presence of smaller or larger masses of chains matted together. Subcutaneous inoculation with artificial cultivations produces no perceptible disorder, but by feeding sheep with a twentieth generation the typical disease has been reproduced, viz., vesicles and ulcerations upon the feet. From the vesicles of such animals lymph was obtained which, on cultivation, yielded the same micrococci, characterized by the same slow growth and the same typical appearance as those used for the experiment. Dr. Klein claims, therefore, that there can be no question about the identity of this peculiar micrococcus with the cause of the disease.

The description thus given of the mode of growth and appearance of the micrococci of foot-and-mouth disease does not materially differ from that given, by the same investigator, of the micrococci found in the ulcers of cows affected with a disease which has since been determined to be cow scarlatina. For the sake of instituting a comparison, I will quote his own words with reference to the cultivation and appearance of the bovine scarlatinal streptococcus.

"From the deeper parts of an ulcer of cow IV. (one he had under observation) material was obtained, with which tubes containing either solid nutritive gelatine or agar-agar mixture were inoculated. After some days, and in both media, a micrococcus appeared, the growth of which was extremely characteristic. These are its characters in the nutritive gelatine: After three to six days' incubation at 20° C., the growth made its appearance at the point or line of inoculation, in the form of small points or granules, whitish in color, and tolerably closely placed. During the next few days their number and

size increased. At the end of a fortnight the line of inoculation was visible as a streak of whitish granules or droplets, some large, others small, more or less closely placed. On the surface of the gelatine the growth, like a film of granules, spreads slowly in breadth, but even after months remains small. When inoculated into the depth of the gelatine the channel of inoculation becomes visible as a whitish streak, made up of smaller and larger droplets. The gelatine is not liquefied by the growth. The same characters are assumed by the growth in agar-agar mixture, and in solid serum. The general aspect of the growth in gelatine, in agar-agar, and in serum, is very similar to that presented by the streptococcus of foot-and-mouth disease, but with this difference, namely, that in gelatine tubes the streptococcus of foot-and-mouth disease is a little faster in its growth, and its component granules are a little more distant. Nevertheless, I have tubes of both kinds of organisms in gelatine, and in agar-agar tubes, which cannot be, from their general appearance, easily distinguished. In faintly alkaline broth, or in broth and peptone, the micrococcus of the cow ulcers grows readily, and in the same manner as that of foot-and-mouth disease. But there is one test by which the two kinds of organisms can be very readily distinguished: the streptococcus of foot-and-mouth disease, when grown in milk, does not affect the fluid character of the milk, whereas milk inoculated with the organism obtained from the cow ulcer will, if kept for two days in the incubator at 35° C., have been turned completely solid. This difference is a very striking difference, and a few days' growth in milk suffices for distinguishing without fail between the two. The microscopic examination of a culture in broth peptone, in gelatine, or in agar-agar mixture, shows that the growth consists of spherical micrococci, arranged as diplococci, and as shorter and longer straight, wavy, or curved chains—streptococcus—these latter sometimes of great length.

As regards the shape of the micrococci, the mode of their division, the branchings of the chains, the presence here and there in the chain of a large element among the smaller ones, the organisms of the ulcers hardly differ from the description which I am preparing of the streptococcus of foot-and-mouth disease."[1] It will be observed that the only point of real difference is the effect the growth of the streptococcus of the cow ulcer has upon milk, solidifying it, while the streptococcus of foot-and-mouth is asserted not to produce this effect. In connection with this point the following may be quoted: "But there is one point in which, so far as I know, it (the milk) differs from all other milk, and that is in its coagulation on being boiled, or having its temperature only slightly raised by being mixed with hot gruel," etc. (*Edin. Med. Journal*, 1863, p. 711). "It is a very general opinion among continental veterinarians that, when the milk can be boiled without coagulating, it is no longer dangerous to use; and Hilderbrandt, in Magdeburg, expressly states that he never observed a single case of injury to health from the use of milk which had been boiled without coagulating" (*Gurlt u. Hertwig's Magazine*, vi., p. 179).

It is certainly true that the two diseases ("foot-and-mouth disease" and the "Hendon cow disease") are very similar in some of their clinical features. This will be made manifest when the mode of development and subsequent history of the vesicles which are characteristic of the two diseases shall have been compared. In the following notes some points of similarity between these two affections may be incidentally noted.

When at Deering, Me., some time ago, for the purpose of studying foot-and-mouth disease in cattle, I saw one or two cases which could very easily have passed for "bovine scarlatina," as described by Drs. Klein and Cameron. The vesicles and ulcers upon the teats and

[1] Report on Milk Scarlatina to the Local Government Board, by Dr. E. Klein, London, England, 1886.

udder were the exact counterpart of the word-picture of those seen upon the Hendon cows' udders and teats.

Just here I may say that during the last four years I have been endeavoring to determine: 1st, Whether scarlatina can be generated in the lower animals by inoculation with human scarlatinal virus; 2d, if so, whether such a disease is mild in character; 3d, whether virus furnished in such a manner could, by inoculation, be used as a means of preventing the development of scarlet fever in human beings.

To determine the truth concerning the first inquiry I obtained some blood from a patient who had scarlet fever, and injected thirty drops of it into the right jugular vein of a colt about one year old. I also introduced under the skin of the thorax a blood-clot obtained from the same patient, and caused the colt to swallow about two drachms of pharyngeal mucus. This occurred on May 1, 1883. The temperature gradually rose from 101¼° F. (the temperature of the colt before inoculation) till it reached, on May 12th, 102⅕° F. During the following night the colt lacerated the skin of the chest to a small extent, and immediately thereafter the temperature began, or continued to rise till it reached 103½° F., at 8 P.M., May 13th. The temperature then began to fall, till it stood at 101¼° F., May 16th, 3 P.M. During this time the intermaxillary glands became enlarged and sensitive, the mucous membrane of the nostrils and eyes injected, and from the nostrils there was a discharge of ropy mucus. Thinking that the injury received on the 12th might have interfered with the natural action of the virus by causing a local inflammation and a general rise of temperature, and wishing, if possible, to intensify the effect of the first inoculation, I injected into the jugular vein some pharyngeal mucus from two well-marked cases of scarlatina. The result was an increased redness of the mucous membranes of the nose and mouth, and a mild sore throat, which disappeared with the fading of

the redness of the mucous membranes. The symptoms above given almost entirely disappeared by May 24th. There was no subsequent œdema of the extremities or sheath, nor was there any desquamation of the cuticle.

On June 28, 1883, I enveloped the head of a perfectly healthy colt in a bag containing a chemise which had been worn by a scarlet-fever patient. This I allowed to remain adjusted about seventy-two hours. On July 2d I injected into the left jugular vein, and into a vein of the leg, some human scarlatinal blood. Within forty-eight hours the temperature began to rise, the colt became less active, showing a tendency to remain quiet. On the sixth day (July 8th) she began to cough and swallowed with difficulty. The visible mucous membranes were quite red, and at certain points had somewhat the appearance of the mucous membrane of the pharynx in man when affected with scarlet fever. The intermaxillary glands were enlarged and sensitive, and, when the throat was pressed upon, the colt evinced uneasiness. There was a discharge of tenacious mucus from the nostrils. The pharynx was unnaturally red. On July 9th I introduced some epidermal scales, obtained from a scarlet-fever patient, under the skin of the abdomen, but so far as I could determine they produced no effect. In this case there was a desquamation of the skin at a few points where I had not previously seen an eruption.

In both colts there followed the inoculations sore throat, redness of the mucous membranes of the nostrils, mouth, and pharynx, elevation of temperature above the normal, and in one, desquamation of the cuticle. It seems reasonable, therefore, to believe that a specific disease was produced in both instances, and that the specific disease was scarlatina. Since that time I have inoculated rabbits, dogs, guinea-pigs, and cattle with human scarlatinal matter, and have obtained some very gratifying results, especially in cattle. In May, 1883, I inoculated a calf with human scarlatinal virus by injecting into the general circulation some blood taken from

a well-marked case (a young man with a typical eruption on neck, chest, abdomen, and limbs), and by subcutaneous introduction of the blood into the abdomen. After the lapse of a few hours the skin at and near the point of inoculation (abdomen) became uniformly reddened. The elevation of temperature was very slight. The redness and sensitiveness of the skin increased till May 24th, when I discovered pus at the centre of the area of redness. The temperature at that time was 102⅕° F. The visible mucous membranes were not affected. Recovery complete by June 1st.

Knowing that cows recently calved were supposed to be especially susceptible to scarlatinal contagium, I procured one that had aborted about one week prior to the time of purchase. I inoculated this cow in the udder with some pharyngeal mucus taken from a patient sick with scarlet fever. The day following the inoculation the temperature rose to 102° F. Pulse, 48. On the third day the temperature was 102⅗° F. Pulse, 56. The temperature then began to descend till it reached 101¼° F. on the eighth day. During this time a cough developed, and it was noticed that the animal did not swallow with the same readiness as usual. At the point of inoculation had developed a superficial vesicle, which very soon became filled with purulent contents. Still deeper in the tissues a small abscess formed, which, after discharging its contents, remained open, discharging a small amount of pus. The skin around the seat of the vesicle and abscess was quite intensely reddened. The temperature gradually declined, till finally, on the nineteenth day, it fell to 100¼° F. There was a desquamation of the cuticle near the abscess where the skin had been reddened.

The next cow I inoculated was in the third or fourth month of gestation. The inoculation was made in the udder, and with pharyngeal mucus from a typical case of human scarlatina. Twenty-four hours after the inoculation the temperature began to rise, although slowly. On

the second day the thermometer showed a temperature of 101½° F., and it did not vary from this point till the seventh day, when it fell to 100° F. During this time the udder became reddened, swollen, and tender, and finally suppurated at the point of inoculation. After the pus, which was small in quantity, was allowed to escape, the cavity of the abscess continued for a few days to discharge pus and then gradually healed. There was no sore throat, nor alteration of the mucous membranes. The reddened integument of the udder around the abscess desquamated. A subsequent inoculation of this cow with human scarlatinal virus produced no effect.

I next inoculated a calf with pharyngeal mucus and epidermal scales derived from scarlatinal patients. The inoculation was made in the abdominal region. At the point of the inoculation there very soon appeared a vesicle about as large as a lima bean, which was at first quite clear, but later became filled with sero-purulent matter, and then became yellow in appearance. Coincidentally with the development of the vesicle there was an elevation of temperature, and the appearance of an intense redness of the skin for some distance from the point of inoculation. There was no sore throat. As I wished the contents of the vesicle as a virus with which to inoculate some children, I punctured it, collecting the fluid in a small bottle. After being punctured the vesicle became converted into an ulcer, which gradually healed. The skin near this vesicle desquamated after the redness disappeared. I am led to believe, as a result of what I have seen while experimenting thus with cattle, that it is possible to infect them with human scarlatinal contagium.

To answer the second question, I may say that, so far as my experience serves me, the lesion produced in the lower animals by inoculation with human scarlatinal virus is a mild one. I am aware, however, that it *might* be otherwise.

In a recent letter Dr. E. Klein, of London, Eng-

land, whose reputation and skill as an investigator place him very high in our esteem and confidence, tells me that cows inoculated with scarlatinal micrococci of human source become affected in *precisely* the same manner as the Hendon cows had been. The disease he refers to has the following characteristics, viz.: "Upon the teats and udder vesicles or bullæ appear, from five to seven days after the commencement of the disease. In number they vary from two to four on a teat, and range in size from a pea to a horse-bean, and contain at first a clear fluid. The first vesicle frequently appears between the two foreteats, close to the abdominal vein. These vesicles usually become broken in milking, leaving raw sores, sometimes red, in other cases pale in color, with raised, ulcerated-looking edges. Shortly after the vesicle becomes ruptured a brown scab forms upon the sore. A thin, watery fluid exudes from under the scab. The skin about the eyeballs is puffy, and is said to present a minute red eruption or rash. There is also an eruption on the hind-quarters. This eruption in its later stages consists of patches of eczematous-looking crusts, which, when picked off, leave a raw, moist sore. The hair comes away with the scab. There is no pitting of the skin. There is sometimes a discharge of yellow matter from the nostrils and eyes. The fever is moderate. Sore throat is said to occur in severe cases. The bowels are loose in very acute cases. There is a dry, husky, irritative cough, with bronchial râles and quickened breathing in some cases." In December, 1885, it was reported that a sudden and extensive outbreak of scarlet fever had occurred in South Marylebone, and that it appeared to be associated with the distribution of milk from a particular retailer. It was afterward discovered that the milk was obtained from cows affected with the disease just described. There was in all about one hundred cases of scarlet fever caused by drinking the infected milk. If, then, it be true that the Hendon cows furnished a contagium which caused the develop-

ment of genuine scarlatina in about one hundred persons, it must be true that the cows had scarlatina ; and again, if the inoculation of cattle with human scarlatinal virus produces a disease identical with the Hendon cow disease, it follows that scarlet fever can be generated at will in susceptible animals.

I have found that results I obtained in several instances are greatly strengthened by the recent experimental investigations of Dr. Klein as to the nature of the Hendon cow disease, and its connection with the outbreak of scarlet fever at South Marylebone and in a certain district in London. The vesicles upon the udder of the cow and the abdomen of the calf already alluded to, as well as the general course of the disease, as occasioned by inoculation with human scarlatinal virus, correspond with the description of the disease as seen in England.

The answer to the third and most important question may perhaps be suggested in what follows :

In the early part of the year 1883 I inoculated twelve persons with virus obtained from horses supposed to have scarlatina. Since that time not one of that number, so far as I can learn, has had scarlet fever. These twelve persons were also inoculated with human scarlatinal blood after they had been inoculated with equine virus. During the summer of the same year I inoculated thirteen children, all of whom had been, and were at the time of inoculation, exposed to the influence of air contaminated by the breath and exhalations of scarlatinal patients. Five of this number escaped, the remaining eight developed the disease (scarlatina) very soon after inoculation, in one instance within five hours. Four of the eight cases had no angina, but simply the eruption, with slight disturbance of the stomach. They were not confined to bed one hour. None of the cases were severe. During the last year I have inoculated two children with the contents of a vesicle produced in the abdomen of a calf by inoculation with virus derived from a patient who had scarlet fever. The notes of the first

case are furnished by Dr. Stubbert, of Bloomfield, N. J., who watched the patient from day to day after the inoculation. "On April 25th the child was inoculated in the left arm with scarlatinal matter taken from a calf. On the 27th an erythematous blush appeared about the scarification. By the 28th the blush had disappeared, but a scab had formed, and around its puffed-up border there was a red areola. On April 30th the child had quite a high fever. On May 1st there appeared on the upper part of the chest a rash similar to a scarlatinal rash. On May 2d the scab came off. The rash which began upon the chest spread to the arms. On May 3d the rash was less bright, and on the right shoulder there was evidence of a slight exfoliation of the skin. In three or four days after this the child was restored to perfect health." The second child was inoculated in the presence of Dr. Stubbert, who kindly permitted me to test the virus not only in this, but in the previous instance. The only result I obtained in this second case was a slight erythematous blush, which, after existing two or three days, gradually disappeared. There was no systemic disturbance. With scarlatinal virus modified by transmission to the cow, I inoculated two other children, producing in them a distinct local lesion. These children have not since developed scarlet fever, although the disease has existed in their immediate neighborhood, and they have been more or less exposed to its influence. While the subject-matter of this paper thus presented to you does not furnish a positive answer to the question, "Can we prevent the development of scarlet fever by the use of virus obtained in one of two ways, as indicated above," it does offer some truthful statements which suggest an answer, and which, I trust, will incite the profession to aid me in the further prosecution of this very interesting and important line of investigation.